REMARKS

I. Introduction

Claims 34-39, 41-68 are pending in the application. Of the above claims, 39, 41-43 and 51-64 are withdrawn from consideration. Claims 65-68 are new. Support for the new and amended claims may be found throughout the specification as filed. No new matter has been added.

Applicant thanks the Examiner for the telephonic interview which took place on January 24, 2008. Examiner Aeder and attorney Blair R. Lanier, Registration No. 56,910, were present. Amendments to overcome the 35 U.S.C. §112 rejection were discussed. None of the amendments discussed were found to place the claims in condition for allowance.

II. Rejection under 35 U.S.C. §112

The Examiner rejects claims 34-38 and 44-50 under 35 U.S.C. §112, first paragraph as failing to comply with the written description and enablement requirements. The Examiner argues that there is a large degree of variation between SEQ ID NO: 1 and the genus of transketolase like-1 genes whose complement hybridizes under stringent conditions to SEQ ID NO: 1. The Examiner further compares the method claims of the instant invention to claims directed to DNA constructs that were found not to meet the written description requirement in U.S. Patent 4,652,525 at issue in *University of California v. Eli Lilly*, 119 F.3d 1559, 1568 (Fed. Cir. 1997),.

Applicant respectfully asserts that the construct claims from *Eli Lilly* are not directly comparable to the method claims of the instant invention. In *Ei Lilly*, the court found that when experiments had been directed to a construct made from a **rat** insulin DNA sequence, not all constructs comprising insulin DNA sequence of **any vertebrate** were enabled. However, the instant claims differ from the construct claims of *Eli Lilly* for at least the reason that the instant claims are method claims of measuring a level of polynucleotides drawn from a single individual, so therefore the concern of genes from different species functioning in different manners does not arise. Further, the instant claims are not directed a construct which may not function due to variation in the sequence, but rather drawn to a method of detecting transketolase like-1 genes, which could be expected to have some amount of variation in their sequence while maintaining functionality. To follow the claimed method, an expert in the field would measure the results level of polypeptides in the biological test sample that hybridize to probes specific for

transkeolase like-1 gene, without necessarily ascertaining the exact sequence of the polynucleotides that hybridize to the probes.

Applicant further asserts that the claims as currently amended to recite "probes specific for a transketolase-like 1 gene" meet the written description requirement. The following passages from the specification support the amendments to claim 34:

> Nucleic acids as used in the context of the present invention may be all polynucleotides, which hybridise to probes specific for the transketolase like-1 sequences used herein under stringent conditions. *WO 03/089667 p. 7 line 30-32.*

> The primers according to the present invention specifically hybridise to the sequence disclosed herein or a part thereof under conditions suitably applied in the course of a nucleic acid amplification reaction but do not hybridise to an other transketolase or transketolase like sequence. *WO 03/089667 p. 9 line 30- p. 10 line 1.*

> Dissections of tumor biopsies can be semi quantitatively analysed for the mRNA level of human transketolase-like-1 gene[.] *WO 03/089667 p. 36 line 6.*

To require that claim 34 recite detecting levels of "polynucleotide SEQ ID NO: 1" rather than "polynucleotides that hybridize under stringent conditions to probes specific for a transketolase-like-1 gene, wherein the probes hybridize to SEQ ID: 1 under stringent conditions," would result in a claim unnecessarily narrow in view of the disclosure set forth in the specification.

Specifically regarding the enablement rejection, the Examiner argues that the claims as previously submitted were not drawn to detecting expression of TKTL1 specifically among the three transketolase genes, TKT, TKTL1 and TKTL2. Rather, the Examiner asserts, that as evidenced by the newly submitted teachings of Langbein et al (British Journal of Cancer 2006,

1-8) TKT, TKTL1, and TKTL2 are highly similar and would all have complements that may hybridize under stringent conditions to SEQ ID NO: 1. The Examiner further argues that detecting *underexpression* of TKTL2 would be indicative of colon cancer, whereas in the claimed method, *overexpression* of TKTL1 is indicative of cancer. The Examiner argues that due to the similarity of the TKT, TKTL1 and TKTL2 genes, the claims could not be practiced as broadly as claimed with any predictability of success.

In response, Applicant submits the article Coy et al., "Molecular Cloning of Tissue-specific Transcripts of a Transketolase-Related Gene: Implication for the Evolution of New Vertebrate Genes." Genomics 32, 309-316, Article No. 0124 (1996). In this paper the authors demonstrate that under hybridization conditions as described in the paper, the TKTL1-cDNA-sequence probe does not hybridize with TKT-sequences or with TKTL2-sequences. Hence, at the time of filing, probes specific for TKTL1, as recited in claim 34, were known in the art. For the Examiner's reference, in the paper Coy et al., the term "TKTL1" as used in the application is referred to as "TKR", and "TKT" as used in the application is referred to as "TK".

The TKTL1-gene is expressed specifically only in certain tissues and cell types. The paper sets forth a procedure to detect the presence of TKTL-1 as follows:

> Hybridizations were carried out in hybridization buffer (0.5 M phosphate, 7% SDS, 0.2% BSA, 0.2% PEG 6000, 0.05% polyvinylpyrrolidone 360,000, 0.05% Ficoll 70,000, 0.5% dextran sulfate) on nylon membranes (Hybond- N Plus, Amersham). Nonspecifically bound probe was removed by washing at 65°C in 40 mM sodium phosphate, pH 7.2, 1% SDS for 60 min. *page 310, left col., lines 3-9.*

The results of the above procedure are shown in Fig. 1a and 1b. Due to the different sizes of the TKT, TKTL1 and TKTL2 transcripts, the three genes can be discriminated by the size of their transcripts by using, e.g., Northern blot technique represented in Fig 1a and 1b. From Fig. 1a and 1b of Coy et al., it is apparent to one of skill in the art that a small transcript of the TKTL1-gene (1350 bp) is highly expressed in the human heart. A hybridization band with a size in the range of that of the TKT-mRNA (ca. 2060 bp) or the TKTL2-mRNA (ca. 2837 bp) occurs neither in the fetal nor in the adult heart tissue. The band that occurs has a size of about

ca 1350 bp. Due to the absence of the large TKTL1 transcript (2500bp) in fetal and adult heart, the cross hybridization of radio-labeled TKTL1 mRNA sequences to TKT or TKTL2 sequences can be evaluated in fetal and adult heart tissue. In fetal and adult heart mRNA a transcript of the size of the TKT or the TKTL2 gene is not being detected, demonstrating that TKTL1 mRNA sequences did not hybridize with TKT or TKTL2 mRNA sequences. Hence, in accordance with Coy et al., probes specific for TKTL1 over TKT and TKTL2 under stringent conditions were known in the art at the time of filing.

Therefore, by utilizing the probes of Coy et al. under stringent hybridization conditions, Coy et al. enables the skilled artisan to carry out a specific and selective hybridization with the TKTL-1-gene, thereby excluding the occurrence of cross-hybridizations with other transketolase-mRNAs. Hence, even if the analysis of the claims of the US 4,652,525 patent from *Eli Lilly* as discussed above is applicable, one of skill in the art would have knowledge at the time of filing of protocols providing hybridizing conditions and probes specific for the genus of the transketolase-like-1 gene which do not hybridize with the TKT and TKTL2 sequences.

Applicant further notes that the passage the Examiner cites to conclude that TKT, TKTL1 and TKTL2, would hybridize to each others' complements under stringent conditions (Langbein et al., British J. of Cancer 2006, 1-8 at left column of page 3), states that "TKTL1 is one of three highly similar transketolases encoded by three separate genes." The Examiner does not point to a specific passage indicating that the three transketolase genes would hybridize to each others' complements under stringent conditions. Like the authors of Coy et al., discussed above, the authors of Langbein et al., utilized techniques that specifically discriminate between the three transketolase genes. *Langbein et al, left col. page 3.*

In view of the above remarks, Applicant respectfully submits that the claims as currently amended are fully enabled and fully supported by the written description. In view of the foregoing remarks, Applicant respectfully requests that the Examiner withdraw the rejections under 35 U.S.C. §112.

V. CONCLUSION

In view of the foregoing, reconsideration and withdrawal of all rejections and allowance of the application is respectfully solicited.

If the Examiner believes that a telephone conversation with the Applicant's attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned, Blair R. Lanier, at the telephone number shown below.

The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMAN SENTERFITT

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